

## AMENDMENTS TO THE SPECIFICATION:

Please replace page 111, paragraph [00284] of the original specification as filed with the following amended paragraph:

The 103 kD band was excised from Coomassie blue stained gel, destained for few hours in 25 mM ammonium bicarbonate/40% ethanol and washed with a sequential increasing percentage of acetonitrile. Proteins were in gel-digested overnight at 30°C with trypsin (Promega, Madison WI) at a concentration of 12 ng/ml in a 25 mM ammonium bicarbonate/10% acetonitrile solution. Peptide mass fingerprinting (PMF) was performed on a Bruker ReflexIII™ matrix-assisted laser desorption/ionization (MALDI) mass spectrometer using  $\alpha$ -cyano-4-hydroxycinnamic acid (Bruker Daltonics Billerica, MA) as a matrix. The mass spectra were externally calibrated with a mixture of 7 standard peptides in the range between 1000 to 3000 Da. Data generated were subjected to database (NCBI) searching using as programs Mascot (<http://www.matrixscience.com>) and ProFound (<http://prowl.rockefeller.edu/>) allowing up to 1 missed trypsin cleavage and a mass tolerance of  $\pm 0.2$  Da. Mass spectrometry was used to determine the identity of nucleolin.

Please replace page 27, paragraph [0079] of the original specification as filed with the following amended paragraph:

The soluble tissue protective cytokine receptor complex ligand may also be recombinantly expressed and utilized in non-cell based assays to identify compounds that bind to the tissue protective cytokine receptor complex ligand. Alternatively, a ligand binding domain of the recombinantly expressed tissue protective cytokine receptor complex, or a fragment of the tissue protective cytokine receptor complex, can be used in the non-cell based screening assays. In another alternative embodiment, peptides corresponding to one or more of the binding domains of the tissue protective cytokine receptor complex, or fusion proteins containing one or more of the binding domains ~~{Please provide residue numbers for binding domains of receptors}~~ of the tissue protective cytokine receptor complex can be used in non-cell based assay systems to identify compounds that bind to the cytoplasmic portion of the tissue protective cytokine receptor complex; such compounds may be useful to modulate a signal transduction pathway of the tissue protective cytokine receptor complex. In non-cell based assays the recombinantly expressed tissue protective cytokine receptor complex is attached to a solid substrate such as a test tube, microtiter well or a column, by means well known to those in the art (see Ausubel *et al.*, 1998, Current Protocols in

Molecular Biology, John Wiley & Sons, NY). The test compounds are then assayed for their ability to bind to the tissue protective cytokine receptor complex.

Please replace page 62, paragraph [158] of the original specification as filed with the following amended paragraph:

In one embodiment of the invention,  $\beta$ c receptor (-/-) knock-out animals are used in assays to identify pathways and/or compounds that involved in a tissue protective activity. For example, normal and  $\beta$ c receptor (-/-) knock-out animals may both be administered an agent or force known to cause tissue damage, *e.g.*, ischemia. Both animals may then be administered a compound and the tissue protective activity of the compound can be determined. Methods for determining a tissue protective activity are well known to those in the art and examples of such methods are disclosed in PCT publication no. WO02/053580, which is incorporated by reference herein in its entirety. If a tissue protective activity is observed in the normal animals but not in the  $\beta$ c receptor (-/-) knock-out animals administered the same compound, then a compound with tissue protective activities dependent on the  $\beta$ c receptor is identified. Further investigation into the identified  $\beta$ c receptor dependent tissue protective pathway may consist of determining if the compound binds to the  $\beta$ c receptor or complexes thereof, or identifying proteins or mRNA transcripts present only in the animals exhibiting the tissue protective activity. Applicants hypothesize that secondary or redundant pathways for tissue protection may be present and that  $\beta$ c receptor (-/-) knock-out animals could be used to investigate such pathways.

~~{Please provide other methods for characterizing tissue protective pathways}~~